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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,151	01/06/2006	JoAnn Burkholder	5051-660	2957

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
03/31/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,151	BURKHOLDER ET AL.	
	Examiner	Art Unit	
	VANESSA L. FORD	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9 and 11-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,9 and 11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This Office action is responsive to Applicant's amendment and response filed January 26, 2009. Claims 1-7 and 10 have been canceled. Claim 8 has been amended. Claims 15 and 16 have been added. Claims 8-9 and 11-16 are under examination.

Rejections Withdrawn

2. In view of Applicant's amendments and remarks the following objection/ rejections are withdrawn:

a) objection of claim 8, page 3, paragraph 2.

b) objection of claim 8, page 3, paragraph 3.

c) Rejection of claims 8-9 ands 12-13 under 35 U.S.C 102(b), pages 4-5, paragraph 5.

Objection Maintained

3. The objection of claim 13 is maintained for the reasons set forth on page 4, paragraph 4 of the previous Office Action. The objection is reiterated below:

Claim 13 is objected to because of the following informality: "*Pfiesteria piscicidae*" should be changed to "*Pfiesteria piscicida*". Correction is required.

This rejection is maintained until corrections are made.

Rejections Maintained

4. The rejection of claims 8-9, 11-13 and newly submitted claims 15-16 under 35 U.S.C. 103(a) is maintained for the reasons set forth on pages 6-10, paragraph 6 of the previous Office Action. The rejection is reiterated below:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The claims are rejected under 35 U.S.C. 103(a) as unpatentable over Moeller et al *(Environmental Health Perspectives, Vol.109, Supplement 5, October 2001)* in view of Larson et al *(The Journal of Biological Chemistry, Vol. 263, No.22, August 5, pp. 10780-10798)* and further in view of Watanabe et al *(Journal of Lipid Research, Vol. 22, 1981, p. 1020-1024)*.

Independent claim 8 is drawn to a method of isolated and purified *Pfiesteria* toxin comprising the steps of (a) culturing a *Pfiesteria* species in a growth media to produce *Pfiesteria* toxin therein; (b) separating a first fraction of organic compounds including said *Pfiesteria* toxin from said growth media; (c) separating a second fraction consisting essentially of said *Pfiesteria* toxin from first fraction by chromatography with porous silica beads, wherein said porous silica beads are Iatrobeads.

Dependent 11 is drawn to the method of claim 8, wherein said porous silica beads are 6RS-8060 Iatrobeads".

Independent claim 15 is drawn to a method of isolated and purified *Pfiesteria* toxin comprising the steps of (a) culturing a *Pfiesteria* species in a growth media to produce *Pfiesteria* toxin therein; (b) separating a first fraction of organic compounds including said *Pfiesteria* toxin from said growth media; (c) separating a second fraction consisting essentially of said *Pfiesteria* toxin from first fraction by chromatography with porous silica beads wherein porous silica beads are Iatrobeads; said second fraction is characterized by an NMR spectrum as given in Figure 1 herein and said *Pfiesteria* species is selected from the group consisting of *Pfiesteria piscicida* and *Pfiesteria shumwayae.*

Dependent claim 16 is drawn to the method of claim 15, wherein said porous silica beads are 6RS-8060 Iatrobeads.

Moeller et al teach a method of isolating and characterizing *Pfiesteria piscicida* toxin (see the Abstract). Moeller et al teach that *Pfiesteria piscicida* was cultured in culture medium (saltwater (SW/Instant Ocean)(Materials and Methods section, page 740). Moeller et al teach that the cell mass (first fraction, claim 8) as well as the filtered SW medium (second fraction, claim 8) were processed separately from subsequent extraction workup and testing (page 740). Moeller et al teach that the cell mass (first fraction) was extracted using pore size silica gel and analyzed by nuclear magnetic resonance spectroscopy (NMR)(page 740). Moeller et al teach that the seawater medium (second fraction) was extracted through a glass-column chromatography using silica as the solid phase in a fashion identical to that described for the cell mass (page 740). Moeller et al teach that all semipurified and purified compounds derived in the isolation schemes were submitted for structural analysis and chemical characterization using gas chromatography-MS (GC-MS) and (NMR)(page 741).

Moeller et al do not teach the claim limitations "the method of claim 8, wherein said porous silica beads are Iatrobeads" or "the method of claim 8, wherein said porous silica beads are 6RS-8060 Iatrobeads".

Larson et al teach that 6RS-8060 Iatrobeads can be used to separate glycolipids in isolation and purification processes (page 10791, 2nd column).

It would been *prima facie* obvious at the time the invention was made to modify the method of isolating an purifying *Pfiesteria piscicida* toxin as taught by Moeller et al to use the 6RS-8060 Iatrobeads as taught by Larson et al because Moeller et al teach that *Pfiesteria piscicida* comprises a lipophilic portion (page 739) and Watanabe et al teach that the solvent system using a column packed with silica gel (Iatrobeads) is used to extract glycolipids and also provides the advantage of being non-toxic as compared with the chloroform-methanol system which is highly toxic (page 1024, 1st column). It would be expected, absent evidence to the contrary, that the use of Iatrobeads as taught by Larson et al and Watanabe et al would be effective in separating glycolipids or lipophilic portions without resulting in a product which is highly toxic.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to isolate and purify *Pfiesteria* toxin. See Moeller et al. It is known in the art to use Iatrobeads (6RS-8060 Iatrobeads) to separated and purify glycolipids. See Watanabe et al and Larson et al. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

Thus, the combination of prior art references as combined provided a *prima facie* case of obviousness, absent convincing evidence to the contrary.

Applicant's Arguments

Applicant urges that the prior art relied upon, must contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references. Applicant urges that the proposed modification or combination of the prior art must have a reasonable expectations of success, determined from the vantage point of the skilled artisan at the time the invention was made. Applicant urges that the prior art reference or combination of references must teach or suggest all of the limitations of the claims.

Applicant urges that to maintain an obviousness rejection under KSR, the action must provide adequate reasoning regarding the predictability and reasonable expectation of success of the claimed invention by one of ordinary skill in the art in the view of the prior art. Applicant urges that when making a determination of obviousness, it should be on what a person of ordinary skill in the art would have known at the time of the invention was made and on what such a person would have reasonably expected in view of that knowledge.

Applicant urges that combining known prior art elements is not sufficient to render the claimed invention obvious if the result should have been predictable to one of ordinary skill in the art.

Applicant urges that the references do not disclose a structure or clear characterization of the active compound (e.g. in such detail as an NMR spectrum) and does not provide complete details of a method of making thereof.

Applicant urges in the instant case, no reasonable expectation of success is obtained because *Pfiesteria* toxin is foremost a water-soluble molecule. Applicant urges that Moeller et al recite that the compound is "a bioactive polar compound" and repeatedly refers to unidentified active a compound as being "polar" and "water soluble". Applicant urges that this would not lead one to rely upon an minor lipophilic portion. Applicant urges that future research will indoubtedly focus on the isolation, purification and characterization of the *Pfiesteria* toxin(s). Applicant urges that this will improve existing methods and aid researchers in developing new methods to detect the presence of the toxin in laboratory and field samples. Applicant refers to C. Rubin et al to support their positions.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 26, 2009 have been fully considered but they are not persuasive.

In response to applicant's argument that there is no case of *prima facie* established, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Moeller et al teach a method of isolating and characterizing *Pfiesteria piscicida* toxin. Moeller et al

teach that *Pfiesteria piscicida* contains a lipophilic-soluble portion as well as a polar extracts (page 739, 3rd column, page 741, 3rd column). Moeller et al teach that all semipurified and purified compounds derived in the isolation schemes were submitted for structural analysis and chemical characterization using gas chromatography-MS (GC-MS) and (NMR)(page 741). Moeller et al do not teach the claim limitations "the method of claim 8, wherein said porous silica beads are Iatrobeads" or "the method of claim 8, wherein said porous silica beads are 6RS-8060 Iatrobeads". Larson et al teach that 6RS-8060 Iatrobeads can be used to separate glycolipids in isolation and purification processes (page 10791, 2nd column). One of ordinary skill in the art would be motivated to modify the method of Moeller et al to include the 6RS-8060 Iatrobeads as taught by Larson et al because Moeller et al teach that *Pfiesteria piscicida* comprises a lipophilic portion (page 739) and Watanabe et al teach that the solvent system using a column packed with silica gel (Iatrobeads) is used to extract glycolipids and also provides the advantage of being non-toxic as compared with the chloroform-methanol system which is highly toxic (page 1024, 1st column).

To address Applicant's comments regarding *KSR International v. Teleflex*, No. 04-1350, slip op. at 4 (U.S. Apr. 30. 2007) ruling, it is obvious to combine the use of silica beads such as 6RS-8060 Iatrobeads as taught by Larsen et al to separate glycolipids in isolation and purification processes because Watanabe et al teach that the solvent system using a column packed with silica gel (Iatrobeads) is used to extract glycolipids and also provides the advantage of being non-toxic as compared with the chloroform-methanol system which is highly toxic. Based on KSR, it would have been

obvious for a person of ordinary skill in the art to use Iatrobeads such as 6RS-8060 Iatrobeads to isolated *Pfiesteria piscicida* toxin because Moeller et al teach that *Pfiesteria piscicida* comprises a lipophilic portion and Watanabe et al teach that the solvent system using a column packed with silica gel (Iatrobeads) is used to extract glycolipids. Therefore, it is obvious to use known techniques in known methods that yield predicable results. Clearly, there is motivation to combine the teaching of the prior art references. Additionally, Applicant has not presented any secondary evidence to show that the combination of prior art references do not teach the claimed invention.

To address Applicant's comments regarding the combination of prior art references not teaching the claims invention, as stated above, the combination of prior art references teach a method of isolating and purifying *Pfiesteria* toxin.

To address Applicant's comments regarding bioactive polar compound of Moeller et al, as stated above, Moeller et al teach that *Pfiesteria piscicida* contains a lipophilic-soluble portion as well as a polar extracts (page 739, 3rd column, page 741, 3rd column). Thus, there is no reason why a person of ordinary skill in the art would not have been lead to use silica beads such as 6RS-8060 Iatrobeads to isolate and purify the lipophilic portion of the *Pfiesteria* toxin based on the teaching of the cited prior art references.

To address C. Rubin et al, it should be noted that this article was published in October 2001. Moeller et al was published in October 2001 as well. Therefore, C. Rubin et al disclose that future research will indoubtedly focus on the isolation, purification and characterization of the *Pfiesteria* toxin(s). Applicant urges that this will improve existing methods and aid researchers in developing new methods to detect the

presence of the toxin in laboratory and field samples. However, at about the same time, Moeller et al published a document teaching a method of isolating and characterizing *Pfiesteria piscicida* toxin. Thus, the *Pfiesteria piscicida* toxin has been isolated and characterized.

In view of all of the above, this rejection is maintained.

5. The rejection of claim 14 under 35 U.S.C. 103(a) is maintained for the reasons set forth on pages 9-10, paragraph 7 of the previous Office Action. The rejection is reiterated below:

Claim 14 is rejected under 35 U.S.C. 103(a) as unpatentable over Moeller et al, Larson et al and Watanabe et al as applied to claims 8-9, 11-13 and 15-16 above and further in view of Glasgow et al (*Phycologia, Volume 40(3), August 13, 2001, p. 234-245).*

Dependent claim 14 is drawn to the method of claim 8, wherein said *Pfiesteria* species is *Pfiesteria shumwayae.*

The teachings of Moeller et al, Larson et al and Watanabe et al have been described previously.

Moeller et al, Larson et al and Watanabe et al do not teach the claim limitation "wherein method of claim 8, wherein said *Pfiesteria* species is *Pfiesteria shumwayae".*

Glasgow et al teach a second species of ichtyotoxic *Pfiesteria* which is named *Pfiesteria shumwayae Glasgow & Burkholder sp.nov.*(see the Title and the Abstract). Glasgow et al teach that both species of *Pfiesteria* species (*Pfiesteria piscicida) and Pfiesteria shumwayae)* have attraction to live fish and their fresh tissues (page 242 (2nd column). Glasgow et al teach that both *Pfiesteria* species toxins are bioactive compounds that cause fish stress, disease and death (page 242, 2nd column).

It would been *prima facie* obvious at the time the invention was made to modify the method of isolating and purifying *Pfiesteria* toxin as taught by Moeller et al to include isolation and purification of *Pfiesteria piscicida* as well as *Pfiesteria shumwayae* because Glasgow et al teach that both *Pfiesteria* species toxins are bioactive compounds that cause fish stress, disease and death (page 242, 2nd column). It would have been obvious, absent evidence to the contrary, that the isolation and purification method as combined above would be effective in isolating and purifying toxin from *Pfiesteria piscicida* and *Pfiesteria shumwayae.*

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to isolate and purify *Pfiesteria* toxin. See Moeller et al. It is known in the art to use latrobeads (6RS-8060 latrobeads) to separated and purify glycolipids. See Watanabe et al and Larson et al. It is further known in the art that there are two species of *Pfiesteria* (*Pfiesteria piscicida* and *Pfiesteria shumwayae)* which are toxin producers that affect fish. See Glasgow et al. It would be obvious to isolate and purify the toxins from *Pfiesteria piscicida* as well as *Pfiesteria shumwayae* . Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

Thus, the combination of prior art references as combined provided a *prima facie* case of obviousness, absent convincing evidence to the contrary.

Applicant's Arguments

Applicant urges that the claims are obviated for the reasons set forth above.

Examiner's Response to Applicant's Arguments

Applicant's arguments filed January 26, 2009 have been fully considered but they are not persuasive.

The teachings of Moeller et al, Larson et al and Watanabe et al have been described previously.

Moeller et al, Larson et al and Watanabe et al do not teach the claim limitation "wherein method of claim 8, wherein said *Pfiesteria* species is *Pfiesteria shumwayae".*

Glasgow et al teach a second species of icthyotoxic *Pfiesteria* which is named *Pfiesteria shumwayae Glasgow & Burkholder sp.nov.*(see the Title and the Abstract). Glasgow et al teach that both species of *Pfiesteria* species (*Pfiesteria piscicida) and Pfiesteria shumwayae)* have attraction to live fish and their fresh tissues (page 242 (2nd

column). Glasgow et al teach that both *Pfiesteria* species toxins are bioactive compounds that cause fish stress, disease and death (page 242, 2nd column).

One of ordinary skill in the art would have been motivated to modify the method of isolating and purifying *Pfiesteria* toxin as taught by Moeller et al, Larson et al and Watanable et al combined above to include isolation and purification of *Pfiesteria piscicida* as well as *Pfiesteria shumwayae* because Glasgow et al teach that both *Pfiesteria* species toxins are bioactive compounds that cause fish stress, disease and death (page 242, 2nd column). It would have been obvious, absent evidence to the contrary, that the isolation and purification method as combined above would be effective in isolating and purifying toxin from *Pfiesteria piscicida* as well as toxin from *Pfiesteria shumwayae.*

This rejection is maintained for the reasons stated above. See paragraph 4.

Status of Claims

6. No claims are allowed.

7. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANESSA L. FORD whose telephone number is (571)272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/
Examiner, Art Unit 1645
March 25, 2009

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645